United States
CONSUMER PRODUCT SAFETY COMMISSION
Washington, D.C. 20207

MEMORANDUM

DATE: 9/19/01

TO : Patricia Bittner, HS

Through: Todd A. Stevenson, Acting Secretary, OS

FROM : Martha A. Kosh, OS

SUBJECT: Petition HP 01-3: Petition for Ban on Use of CCA Treated Wood in Playground Equipment

ATTACHED ARE COMMENTS ON THE CH01-4

COMMENT	DATE	SIGNED BY	AFFILIATION
CH01-4-1	7/24/01	Consumers **(approximately) 3,000**	Generation Green P.O. Box 7027 Evanston, IL 60201
CH01-4-2	7/27/01	R. Gilstein	gils4@mediaone.net
CH01-4-3	7/29/01	D. Marcelius	13881 Green Valley Rd Forestville, CA 95436
CH01-4-4	7/30/01	Brian Fink Consumer	390 2nd St., #13 Brooklyn, NY 11215
CH01-4-5	7/31/01	Edward Hoy	1031 Claire Ave Huntingdon Valley, PA 19006
CH01-4-6	7/31/01	Eloise Gumpert	6188 Bellaire Dr. New Orleans, LA 70124
CH01-4-7	7/31/01	Julia Holladay	JuliaLee60@aol.com
CH01-4-8	0/02/01	Emily Sims	forest elf@hotmail.com
CH01-4-9	8/05/01	Marge Folino	keith@glassinc.com
CH01-4-10	8/06/01	C. Stombler	3620 Forest Garden Ave. Baltimore, MD 21207
CH01-4-11	8/09/01	Mark Dobson President	PlayLofts 5200 N. US 1 Melbourne, FL 32940

Petition HP 01-3: Petition for Ban on Use of CCA Treated Wood in Playground Equipment

CH01-4-12	8/09/01	V. Christie	sibleyhouse@hotmail.com
CH01-4-13	8/10/01	Ruthann Spence	ru66@bellsouth.net
CH01-4-14	8/10/01	Thomas French	HC 68 Box 139 Taos, NM 87571
CH01-4-15	8/13/01	Karen Pushinsky	diamond1@fyi.net
CH01-4-16	8/12/01	Robert Davis	40 Puritan Road Tonawanda, NY 14150
CH01-4-17	8/20/01	Jonathan Held	jsheld@hotmail.com
CH01-4-18	8/20/01	Joseph Prager	9409 SW 81st Way Gainesville, FL 32608
CH01-4-19	8/21/01	Terri Becker	507 Lowell #4 Cincinnati, OH 45220
CH01-4-20	8/24/01	Rhonda Ruff	Seminole Tribe of Florida Water Resource Mgmt. 6300 Stirling Road Hollywood, FL 33024
CH01-4-21	9/05/01	Gregory Kidd Science & Legal Policy Director	Beyond Pesticides National Coalition Against the Imsuse of Pesticides 701 E St, SE, Suite 200 Washington, DC 20003
CH01-4-22	9/05/01	Marc Leathers President	Leathers & Associates 99 Eastlake Road Ithaca, NY 14850
CH01-4-23	9/05/01	Nina Derda	2070 19th St Wyandotte, MI 48192
CH01-4-24	9/09/01	W. Oemichen Administrator	Depart. Of Agriculture Trade and Consumer Protection 2811 Agriculture Dr. P.O. Box 911 Madison, WI 53708
CH01-4-25	9/11/01	Gary Ginsberg Ph.D., Toxicologist &	Connecticut Department of Public Health PO Box 340398, MS 11CHA Hartford, CT 06134

Con't		David Stilwell Ph.D.	Connecticut Agriculture Experiment Station PO Box 1106 New Haven, CT 06504
CH01-4-26 (**attachments in OS**)	9/11/01	Sarah Watson **on behalf of The American Chemistry Council and the American Wood Preservers Institute**	Steptoe & Johnson 1330 Connecticut Ave, NW Washington, DC 20036
CH01-4-27	9/11/01	M. Feenster Coordinator - Regulatory Affairs	American Forest & Paper Association 1111 19th St, NW Washington, DC 20020
CH01-4-28	9/11/01	Jeff Hobson	2220-D Sacramento St. Berkeley, CA 94702

CCA pet comment 1

July 24, 2001

Ann Brown, Chairperson
U.S. Consumer Product Safety Commission
Washington, D.C. 20207-0001

Dear Chairperson Brown,

I urge the Consumer Product Safety Commission to implement an immediate ban on the use of CCA (chromated-copper-arsenate) on wood used for wooden play structures. I also urge your agency to begin a review of CCA-treated wood for other uses such as picnic tables and decks. The risks associated with arsenic, especially for children, are unnecessary. Arsenic is carcinogenic, and has been linked to nerve damage and other health problems.

Sincerely,

ARDYCE F EARL
1920 W. WAUGH ST.
GRAND ISLAND, NE 68803-

Brown, Ann W.

CCA wood 2

From: gils4 [gils4@mediaone.net]
Sent: Friday, July 27, 2001 4:45 PM
To: abrown@cpsc.gov
Subject: Ban CCA

Re: Petition HP 01-3
Petition for Ban on Use of CCA-treated Wood in Playground Equipment

Dear Chairperson Brown,

I urge the Consumer Product Safety Commission to implement an immediate ban on the use of CCA (chromated-copper-arsenate) on wood used for wooden play structures. I also urge your agency to begin a review of CCA-treated wood for other uses such as picnic tables and decks. The risks associated with arsenic, especially for children, are unnecessary. Arsenic is carcinogenic, and has been linked to nerve damage and other health problems.

It's your job to protect us.

Sincerely,
Robert Gilstein

Adkins, Patricia H.

CCA wood pet comment 3

From: DebDonovan@aol.com
Sent: Sunday, July 29, 2001 11:44 AM
To: abrown@cpsc.gov
Subject: Re: Petition HP 01-3

Re: Petition HP 01-3

Petition for Ban on Use of CCA-treated Wood in Playground

Equipment

Dear Chairperson Brown,

I urge the Consumer Product Safety Commission to implement an

immediate ban on the use of CCA (chromated-copper-arsenate) on wood used for

wooden play structures. I also urge your agency to begin a review of CCA-treated

wood for other uses such as picnic tables and decks. The risks associated with

arsenic, especially for children, are unnecessary. Arsenic is carcinogenic, and

has been linked to nerve damage and other health problems.

Sincerely,

Deborah Marcelius
13881 Green Valley Rd
Forestville, CA 95436

CCA comment 4

Stevenson, Todd A.

From: Brian Fink [BFink@urbanjustice.org]
Sent: Monday, July 30, 2001 7:07 PM
To: 'cpsc-os@cpsc.gov'
Subject: Petition HP 01-3, Petition for Ban on Use of CCA Treated Wood in Playground Equipment

Office of the Secretary, Consumer Product Safety Commission,
Washington, DC 20207,
cpsc-os@cpsc.gov
Petition HP 01-3,
Petition for Ban on Use of CCA Treated Wood in Playground Equipment

Dear Consumer Public Safety Commission:

Please accept my comments in support of the proposed ban of chromated-copper-arsenate (CCA) treated wood in playground equipment.

A ban is necessary because ``[r]ecent research has shown that arsenic is more carcinogenic than previously recognized, that arsenic is present at significant concentrations on CCA-treated wood and in underlying soil, that the health risks posed by this wood are greater than previously recognized, and that past risk assessments were incomplete.''

I agree that the Commission should review the safety of CCA-treated wood for general use.

Sincerely,

Brian Fink
390 2nd St., #13
Brooklyn NY 11215

July 31, 2001, CCA petition comment 5

Re - Petition # P 01-3
Petition to Ban use of CCA - Treated
Wood in Playground Equipment.

Dear Chairperson Brown,

I urge the Consumer Product Safety Commission to implement an immediate ban on the use of CCA (chromated-copper-arsenate) in wood used for wooden play structures. I also urge your agency to begin a review of CCA-treated wood for other uses such as picnic tables and decks. The risks associated with these uses, especially for children, are unnecessary. Arsenic is carcinogenic, and has been linked to nerve damage and other health problems.

Sincerely,

Edward K. Hoy
1031 Clover Ave
Huntingdon Valley Pa.
19006-8625

2001 AUG -6 A 11:22

RECEIVED OFFICE OF THE SECRETARY

6

7/31/01 pet CCA Comment

Re: petition HP 01-3

Petition for Ban on Use of CCA-treated Wood in Playground Equipment

Dear Chairperson Brown,

I urge the Consumer Product Safety Commission to implement an immediate ban on the use of CCA (chromated-copper-arsenate) on wood used for wooden play structures. I also urge your agency to begin a review of CCA-treated wood for other uses such as picnic tables and decks. The risks associated with arsenic, especially for childred, ~~for~~ are unnecessary. Arsenic is carcinogenic, and has been linked to serve damage and other health problems.

Sincerely

Eloise M Gumpert
6188 bellaire Dr[illegible]
New Orleans LA 70124

CCA wood petition 7

Brown, Ann W.

From: JuliaLee60@aol.com
Sent: Tuesday, July 31, 2001 2:38 PM
To: abrown@cpsc.gov
Subject: Petition HP 01-3

Re: Petition HP 01-3
Petition for Ban on Use of CCA-treated Wood in Playground Equipment

Dear Chairperson Brown,

I urge the Consumer Product Safety Commision to implement an immediate ban on the use of CCA (chromated-copper-arsenate) on wood used for wooden play structures. I also urge your agency to begin a review of CCA-treated wood for other uses such as picnic tables and decks. The risks associated with arsenic, especially for children, are unnecessary. Arsenic is carcinogenic, and has been linked to nerve damage and other health problems.

Sincerely,
Julia Holladay

Brown, Ann W.

From: Emily Sims [forest_elf@hotmail.com]
Sent: Thursday, August 02, 2001 10:17
To: abrown@cpsc.gov
Subject: CCA

Dear Chairperson Brown,

I urge the Consumer Product Safety Commission to implement an immediate ban on the use of CCA (chromated-copper-arsenate) on wood used for wooden play structures. I also urge your agency to begin a review of CCA-treated wood for other uses such as picnic tables and decks. The risks associated with arsenic, especially for children, are unnecessary. Arsenic is carcinogenic, and has been linked to nerve damage and other health problems.

Sincerely,

Emily Sims

CCA wood pt 9

Brown, Ann W.

From: Keith Folino [keith@glassinc.com]
Sent: Sunday, August 05. 2001 6:03
To: abrown@cpsc.gov
Subject: CCA

Dear Sir,

I am writing to ask you to support a ban on the use of CCA on wood used for playground equipment. Children should not be exposed to arsenic unnecessarily. I also don't think it should be used on deck wood or picnic table wood or other situations where people come into contact with it.

Thank you,
Marge Folino

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Mrs. Charlotte Stombler
3620 Forest Garden Ave.
Baltimore, MD 21207-6307

CCA petition comment

Re: Petition HP 01-3
Petition for Ban on Use of CCA-treated Wood in Playground Equipment

Dear Chairperson Brown,

I urge the Consumer Product Safety Commission to implement an immediate ban on the use of CCA (chromated-copper-arsenate) on wood used for wooden play structures. I also urge your agency to begin a review of CCA-treated wood for other uses such as picnic tables and decks. The risks associated with arsenic, especially for children, are unnecessary. Arsenic is carcinogenic, and has been linked to nerve damage and other health problems.

Sincerely,

JD

PlayLofts
5200 N. U.S. 1
Melbourne, FL 32940
(321)752-6111

August 9. 2001

Consumer Product Safety Commission
Washington, D.C. 20207

REGARDING CCA IN PLAYGROUNDS

Please see my enclosed editorial column from Florida Today. Despite the reporters' feeding frenzy over the word "arsenic", pressure treated lumber has not been linked to a single instance of illness in over sixty years of use! It must be recognized that the current controversy has been manufactured by the press.

Florida Today reporter Brian Monroe, when asked why they are going after playsets when the nearby privacy fences have so much more CCA ground-contact, confessed that it's because playgrounds make a "sexy story".

The scientific community has registered protest after protest against these irresponsible reports. As with the Elvis "controversy", the public is caught in the middle. On the one hand, renowned and responsible doctors, scientists, and technicians have concluded after vast research that Elvis Presley is indeed dead. On the other hand, reporters all over the world have been collecting sightings in shopping malls and airports, and even managed to briefly sober up an ex-doctor to have him pronounce that Elvis may be among us. So who is the poor public to believe?

But back to the serious, creating fear to this degree, that a product with not one instance of documented harm is being questioned, has been an act of negligence causing financial and emotional damages. Meanwhile real environmental issues go un-addressed.

Please again affirm that CCA treated lumber is as risk-free as you can ever hope to get for playgrounds, backyard fences, picnic tables, etc. And please include a warning to irresponsible reporters that their tactics are the real threat to consumer safety and the public well-being.

Sincerely yours,

Mark Dobson
President, PlayLofts

Playground Safety
The Making of a Sexy Story

by Mark Dobson

As a concerned parent, you can't watch your network news today without being assaulted by the shock journalism of "Poisonous Playgrounds--story at eleven!" Crafted to appear as an investigative report with your safety in mind, this "story" has been recycled many times and repeatedly put to rest by the scientific community.

In 1997, TV's Hard Copy ran "Poisons in the Playground," with no requirement to follow up with the voluminous protests of toxicology professionals. A panel of scientists objected to the way Hard Copy irresponsibly left viewers with a mistaken impression. Discussing the wood preservative chromated copper arsenate (CCA), Dr. Elizabeth Whelan, president of the American Council on Science and Health, said, "Treated wood offers substantial benefits to consumers and poses no known health hazard."

In media, a "sexy" story is one that can sell the paper that day, or get you to sit through lots of commercials waiting for it to air. While genuine journalists do actual research and check many expert sources, the shock-jocks write exciting headlines and then twist all quotes to fit. The story is basically already written before they interview anyone.

Although the word *arsenic* is liberally socked at you by the News Team, the story about soil levels is an old one. In the consumer information sheet approved by the United States Environmental Protection Agency, care is taken to distinguish between the *arsenate* used in wood preservatives, and the *arsenic* which is not. The EPA reviewed the use of CCA extensively and concluded that the wood did not pose a short or long-term hazard to children on playground equipment, that the agency has not identified any significant health concerns from exposure to residues, and that the wood "did not pose unreasonable risks to children or adults, either from direct contact with the wood or from contact with surrounding soil where some releases may have occurred."

Doctors, toxicologists, and other scientists who contributed to the findings of the ACSH, the EPA, and the Consumer Product Safety Commission, consider the shock journalism harmful in that it simply capitalizes on creating fear, and distracts from real dangers in the environment. You can examine their findings in detail at preservedwood.com and be reassured that your deck, your privacy fence, your picnic table, your dock and your backyard playset are safe for you to enjoy.

Perhaps one day you'll find all your favorite restaurants closed because of "Deadly Chlorine Found In Food!" The News Team knew all along it was the safe sodium chloride. But table salt just isn't a sexy story.

Mark Dobson is the founder and president
of PlayLofts, located in Melbourne, which designs
and installs commercial and backyard play-systems.

Brown, Ann W.

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From: v christie [sibleyhouse@hotmail.com]
Sent: Thursday, August 09, 2001 2:47 PM
To: abrown@cpsc.gov
Subject: Petition HP 01-3

Dear Chairperson Brown, Please implement a ban on the use of arsenic treated wood for the use in playground equipment for children. Children have enough environmental health hazards without addding arsenic to the mixture. Please ban it from future use and set about removing from all playground equipment where it is now in use. Thank you, Virginia Christie

Stevenson, Todd A.

CCA petition comment 13

From: Ruthann [ru66@bellsouth.net]

Sent: Friday, August 10, 2001 5:58 PM

To: cpsc-os@cpsc.gov

Subject: Fw: Petition HP 01-3, Petition for Ban on Use of CCA Treated Wood in Playground

Sent: Friday, August 10, 2001 5:44 PM
Subject: Fw: Petition HP 01-3, Petition for Ban on Use of CCA Treated Wood in Playground Equipment

Sent: Friday, August 10, 2001 4:09 PM
Subject: Petition HP 01-3, Petition for Ban on Use of CCA Treated Wood in Playground Equipment

To the Office of the Secretary
Consumer Product Safety Commission

Re: Petition HP 01-3, Petition for Ban on Use of CCA Treated Wood in Playground Equipment

I strongly support this petition. We have recently removed the play structure in our backyard because it was made from CCA pressure treated wood. We had soil samples taken and tested from around the play structure in April. The arsenic levels came back shockingly high, ranging up to 24.0 (when the acceptable levels, we're told are .08). From the information we've gathered there is much yet to be learned about the long term affects it (CCA treated wood) may have on our children's health as well as the environment. Shouldn't we, the adults, parents and government make every effort to protect the children, especially when we have been given the beginnings of information that shows significant cause for concern.

Sincerely,
Mrs. Ruthann Spence

cca wood pet. comm 14

August 10, 2001

Ann Brown, Chairperson
U.S. Consumer Product Safety Commission
Washington, D.C. 20207-0001
Email: abrown@cpsc.gov

Re: Petition HP 01-3
Petition for Ban on Use of CCA-treated Wood in Playground Equipment

Dear Chairperson Brown,
I urge the Consumer Product Safety Commission to implement an immediate ban on the use of CCA (chromated-copper-arsenate) on wood used for wooden play structures. I also urge your agency to begin a review of CCA-treated wood for other uses such as picnic tables and decks. The risks associated with arsenic, especially for children, are unnecessary. Arsenic is carcinogenic, and has been linked to nerve damage and other health problems.

Sincerely,

Thomas B. French
HC 68 Box 139
Taos, NM 87571
50 758-3827

~~Stevenson, Todd A.~~

CK petition 15

From: n/a [diamond1@fyi.net]
Sent: Monday, August 13, 2001 2:41 PM
To: cpsc-os@cpsc.gov
Subject: Treated Wood

Hello,

My husband worked as a carpenter/homeremodeler for over 25 years. I do know he worked with treated lumber many many times over these years. He died in 98 at age 49. Are you issuing any concerns or doing a study on the construction industry personnel or people in lumber yards etc. who work around or are constantly exposed to this?
I realize no one really wants to get involved especially if it will cost money in the long run but there should be some accountability out there somewhere!!
Thank you.
Karen Pushinsky

CCA put comment 16

August 12, 2001

Ann Brown, Chairperson
US Consumer Product Safety Commission
Washington DC 20207-0001

Dear Chairperson Brown:

I agree with the petition to the United States Consumer Product Safety Commission to ban arsenic treated wood in playground equipment and review the safety of arsenic treated wood for general use.

We have many wooden playgrounds in the Buffalo, New York that are made with arsenic treated wood in playground equipment. I am afraid that this treated wood has or will affect my children and other children in the area. Please stop the use of CCA in playground equipment.

Regards,

Robert Davis

Robert Davis
40 Puritan Road
Tonawanda, NY 14150

ENVIRONMENTAL WORKING GROUP

HEALTHY BUILDING NETWORK
healthybuilding.net

Petition to the United States Consumer Product Safety Commission to Ban Arsenic Treated Wood in Playground Equipment and Review the Safety of Arsenic Treated Wood for General Use

May 22, 2001

Ann Brown, Chairperson
U.S. Consumer Product Safety Commission
Washington, DC 20207-0001

Dear Chairperson Brown:

The Environmental Working Group (EWG), a non-profit research organization, and the Healthy Building Network (HBN), a non-profit advocacy organization, petition the Consumer Product Safety Commission (CPSC) to enact an immediate ban of chromated-copper-arsenate (CCA) treated wood for use in playground equipment and to begin a review of the safety of CCA-treated wood for general use, on grounds that the continued sale of these items violates provisions of the Federal Hazardous Substances Act and the Consumer Product Safety Act.

In 1990, the Consumer Product Safety Commission issued a study on the "Estimate of Risk of Skin Cancer from Dislodgeable Arsenic on Pressure Treated Wood Playground Equipment." The study concluded that the risks to children playing on manufactured playground equipment were small, but that "a possible hazard might be created when playground equipment is built with unfinished pressure-treated wood from retail sources." At the time, the CPSC declined to take any action against the use of CCA-treated wood in playground equipment. However, during the ten years since, many changes in scientific understanding have made clear that playground equipment and other wood treated with CCA poses imminent and unreasonable health risks to consumers, particularly children.

CPSC is urged to consider the following new information:

- A 1999 National Research Council (NRC) study which concluded that arsenic is a much more potent carcinogen than previously recognized, and a cause of other cancers such as bladder and lung cancer in addition to skin cancer.

- Research by the NRC and others since 1990 which has also shown arsenic to be an endocrine disruptor, and has linked arsenic ingestion to immune system suppression, increased risks of high blood pressure, cardiovascular disease, and diabetes.

- Numerous studies conducted since 1990 which have confirmed that significant quantities of arsenic can be dislodged from the surface of CCA-treated wood, that these levels are greater than what even the wood preservatives industry itself has determined to be safe, and that the cancer risk could be as great as 1 in 1,000.

- The 1990 CPSC study which examined the risks posed to children playing on manufactured playground equipment. However, subsequent studies show that playground equipment represents only a small fraction of the places where children may come into contact with treated wood - other places include, for

example, decks, railings, picnic tables, fences and docks. Another exposure pathway that has not been considered by the CPSC and other analyses is ingestion of arsenic-contaminated soil beneath CCA structures.

- There have been two important changes in the market for pressure treated wood used in children's play structures. First, "unfinished" pressure treated wood appears to be more widely used now in these applications. Second, alternatives to pressure treated wood (including composite "plastic lumber" and wood treated with less toxic treatment compounds) are now widely available and have proven performance.

From the weight of the evidence described in this petition, it is clear that the Consumer Product Safety Commission must take immediate action in order to protect American children from playground equipment that is hazardous to their health. In addition, it is clear that the CPSC must further take prompt action to assess the health threats to consumers posed by the general use of CCA-treated wood.

In this petition, EWG and HBN document that:

1. Arsenic is a more potent and broad-acting carcinogen than previously recognized, and a cause of other cancers such as bladder and lung cancer in addition to skin cancer.

2. Exposure to arsenic from CCA-treated wood is more significant than previously recognized.

3. The health risks from CCA-treated wood are more significant than previously recognized. Arsenic is an endocrine disruptor, and has also been linked to immune system suppression, increased risks of high blood pressure, cardiovascular disease, and diabetes.

4. Many exposure pathways besides manufactured playground equipment exist and need to be addressed.

5. Comparable, less toxic alternatives to CCA-treated wood exist.

6. The Consumer Product Safety Act and the Hazardous Substances Act require the CPSC to ban CCA for use in playground equipment and promptly review the safety of other uses.

Background on CCA

Chromated copper arsenate (CCA) is a mixture of chromium, copper and arsenic used to protect wood from insect attacks and fungal decay. It is 22 percent arsenic by weight (Solo-Gabrielle et al. 2000). Recognized to pose unreasonable risks to workers and nearby residents, CCA has been banned by the EPA for all non-wood uses. (EPA 1993) CCA has also been banned for use as a wood preservative by several other countries. In the United States, however, CCA is by far the most common chemical used to produce "pressure-treated" lumber. In 1997, over 90 percent of the treated lumber, timbers, posts, and plywood, and about 75 percent of treated wood volume overall was produced with CCA (Solo-Gabrielle et al. 2000). In 1996, more than 144 million pounds of CCA was used to treat almost 460 million cubic feet of wood. (AWPI 1997) This corresponds to more than 30 million pounds of arsenic, making the United States the world's largest consumer. In fact, the U.S. wood treatment industry uses 50 percent of the arsenic produced worldwide. (USGS 1999) Between 1964 and today, an estimated 550 million pounds of arsenic have been put into pressure-treated wood.

Background on Arsenic

The risks associated with CCA stem from arsenic exposure. When ingested or inhaled, arsenic is readily taken up by the body. But people may be completely unaware of their exposure since this toxic metal is tasteless, colorless and odorless. Arsenic causes a wide range of adverse health effects at high, moderate and low doses.

An ounce of arsenic is enough to kill 250 adults (ATSDR 2000). High levels that are not immediately deadly can cause nerve damage, vomiting, fatigue, diarrhea, nausea and the decreased production of red blood cells. Similar effects can also occur after long term ingestion (5 to 15 years) of arsenic at low to moderate levels. (NRC 1999) Recent research has also linked arsenic ingestion to immune system suppression, increased risks of high blood pressure, cardiovascular disease, and diabetes (NRC 1999).

Regulation concerning the exposure to arsenic in drinking water, however, has focused on the risk of cancer. The current drinking water limit for arsenic (MCL, or maximum contaminant limit) is 50 micrograms per liter (ug/L or ppb), which has been the standard since 1947. A new MCL of 10 micrograms per liter was proposed by the EPA under the Clinton administration, but was suspended by the Bush Administration for further review.

1. Arsenic is a more potent and broad acting carcinogen than previously recognized.

Arsenic is classified by the EPA and the World Health Organization as a known human carcinogen. The association between arsenic ingestion and skin cancer has been recognized for more than a hundred years (ATSDR 2000). In 1990, the Consumer Product Safety Commission evaluated the risks of skin cancer from arsenic exposure through treated wood play structures. Over the past 10 years, however, the scientific picture of arsenic carcinogenicity has changed significantly.

In 1999, the National Research Council reviewed the growing body of evidence that arsenic was even more harmful that previously thought. They concluded that there are indisputable links to skin, bladder and lung cancer, and that there is some evidence to suggest links to kidney and liver cancer. These findings were based on human epidemiological studies in Taiwan, Chile, and Argentina where whole populations were exposed to arsenic in drinking water- notable because such extensive human data is rare (NRC 1999).

The NRC concluded that the current drinking water standard was not adequately protective of public health and "requires downward revision as promptly as possible." In fact, NRC analyses showed that consuming arsenic at the current MCL (or 100 ug of arsenic a day) could lead to a cancer risk of 1 in 100 to 1 in 1,000 (NRC 1999). A Dartmouth College research team also found that arsenic acts as an endocrine disruptor at low concentrations: between 25 and 50 micrograms per liter (Kaltreider 2001).

Recent research has also shown that children metabolize arsenic differently, likely making them more susceptible to its harmful effects. Arsenic is metabolized through a process called methylation which converts the metal into a less toxic form which is easier to excrete. Methylation reduces the amount of time the body is exposed to arsenic's toxic effects. Yet studies have shown that substantial variations exist in people's ability to methylate arsenic, and that children are not able to convert arsenic into less toxic forms as readily as adults (NRC 1999). Furthermore, research has also shown that people with poor nutrition may be more susceptible to arsenic related health effects, meaning that low-income children may be especially at risk from treated wood (NRC 1999).

In light of this new information, it is clear that the question of the cancer risk posed by arsenic treated wood needs to be reevaluated by the CPSC. The cancer slope factor used by the CPSC, for instance, is 3 times lower than what is now used by the EPA (Roberts and Ochoa 2001).

2. Exposure to arsenic from CCA-treated wood is more significant than previously recognized.

The 1990 CPSC study found detectable arsenic on only two of the seven play structure samples tested. However, most of these samples had previously been coated with an oil-based stain. Recent studies indicate that these findings may not be representative of the levels of arsenic that are dislodgeable from the

surface of CCA-treated play structures, decks and other structures that children and adults come into contact with on a daily basis.

A research team from the Connecticut Agricultural Experiment Station looked at arsenic levels on the surface of pressure treated wood boards and municipal play structures. Wipe samples of boards that are typically used for decking found a range of 6 to 122 ug of arsenic per 100 cm^2, with an average of 40 ug/ 100cm^2 (Stilwell 1998). Wipes from horizontal boards of municipal play structures were found to have between 2 and 45 ug of arsenic per 100 cm^2, and averaged 9 ug. Vertical poles were found to have much higher levels, ranging between 5 and 632 ug/100 cm^2, with an average of 105 ug.

Two studies conducted in Canada found surface arsenic levels ranging from 0.05 to 42 micrograms of arsenic per 100cm^2, and averaging 15 and 4.3 micrograms (HWC 1992, Galarneau et al. 1990). Sampling conducted by the Environmental Working Group on two municipal playstructures in California found levels of surface arsenic ranging from 118 to 132 micrograms per 100cm^2.

These results are consistent with a study done by the California Department of Health Services (CADHS 1987) which found a range of 31 to 314 ug/100cm^2 on municipal play structures (no average given) and a mean arsenic level of more than 1000 ug/100cm^2 on a pier. CADHS has also been the only agency to date to look at the amount of arsenic children and adults get on their hands from touching pressure-treated wood. It found that volunteers who rubbed municipal playground wood for five minutes had an average of 236 ug of arsenic on their hands, with levels reaching up to 1,260 ug in one case.

A recent analysis commissioned by the Florida Department of Environmental Protection estimated the daily dose of arsenic associated with exposure to CCA-treated wood from different surface levels of arsenic found in the scientific literature (Roberts and Ochoa 2001). It found that a child might get a dose of 482 ug of arsenic a day if playing on a structure with surface levels of 632 ug of arsenic per 100 cm^2, a dose of 76 ug a day if the structure had arsenic levels of 100 ug/100cm^2, or a dose of 38 ug a day if surface arsenic levels were 50 ug/100cm^2. This is consistent with the CADHS findings which estimate that a child might get a dose of between 24 and 630 ug of arsenic per visit to a play structure made of CCA-treated wood (CADHS 1987).

Taking the results from all studies which have looked at arsenic on the surface of playground equipment (a total of 7 studies and 122 samples), the mean surface arsenic level is 32 ug per 100 cm^2. This has been estimated to correspond to a 24 ug dose of arsenic per day for children, just from playing on CCA-treated play structures (Roberts and Ochoa 2001).

By comparison, the U.S. Food & Drug Administration recently analyzed the typical ingestion of inorganic arsenic through food and found that a six year old child would be consuming an average of 4.6 ug of arsenic per day (Tao and Bolger 1998). Because 90 percent of drinking water systems in the U.S. have arsenic concentrations which are lower than 10 ug/L, and children age 4 through 6 drink an average of 0.45 liters of water a day, most children are ingesting less than 4.5 micrograms of arsenic per day from water (USGS 2000, EPA 2000).

The average child, therefore, is ingesting less than 10 ug of arsenic a day through food and drinking water. A child playing for just a few minutes on treated wood may easily get more arsenic on her hands than she would be ingesting daily from food and water for a day. This fact was recently recognized by the Connecticut Department of Public Health. In a 1998 publication titled "What you need to know about pesticides used in pressure treated wood," the agency states that "exposure from CCA-treated wood can be the major source of arsenic for children who frequently play on CCA-treated playscapes, treehouses, or decks" (CDPH 1998).

It has become evident that significant exposure to arsenic can occur from playing on or handling pressure-treated wood, that these exposures were not adequately assessed in the CPSC's previous analysis, and that these exposures could easily be in excess of those from food and drinking water.

3. The health risks from CCA-treated wood are more significant than previously recognized.

In light of the attention that this issue has received in recent months, the Florida Department of Environmental Protection and the wood treatment industry have taken a new look at the health risks of arsenic in CCA-treated wood. Both studies indicate that the levels of arsenic present on the surface of treated wood put public health at risk.

Commissioned by the Florida Department of Environmental Protection, University of Florida researchers combined data from a number of previously conducted studies to estimate the cancer risk posed to children exposed to CCA-treated wood structures for 5 years during childhood. Including arsenic absorption from skin, and using up-to-date cancer risk assessment factors, they found that the cancer risk from children regularly touching CCA-treated wood ranged from 4 in 100,000 to more than 1 in 1,000 (Roberts and Ochoa 2001). These results are supported by previous work by the California Department of Health Services, which estimated that children faced an additional lifetime skin cancer risk of between 6 in 1,000 to 1 in 10,000 from playing on treated wood play structures (CADHS 1987). At the mean surface arsenic level found on play structures (32 ug/100 cm^2), the researchers shows a cancer risk of 1 in 10,000 for children playing on treated wood for 5 years during childhood (Roberts and Ochoa 2001).

Even the wood preservatives industry's own studies have found that the amount of arsenic on the surface of wood is too high to be safe. Early in 2001, the American Wood Products Institute (AWPI) commissioned and publicized the results of a study to refute media attention showing CCA-treated lumber could be causing harm. In April, however, the industry admitted that the study contained a mathematical error which underestimated the risks by a factor of 1,000. Although the AWPI still maintains that the risks of CCA-treated wood are low, a memo explaining the adjusted values tell a different story (HSWMR 2001, attached). In calculating the amount of arsenic that should be allowed on the surface of wood, the AWPI analysis showed that to protect human health, arsenic levels should be 2 ug per 100 cm^2, a level which is significantly lower than what wipe and hand samples have found.

Numerous cases where consumers have suffered arsenic poisoning from working with CCA-treated wood have also been documented, highlighting the fact that acute risk is present.

- The CADHS began investigating the risk of treated wood in playgrounds after workers building a pier in Monterey, California, developed arsenic poisoning from CCA-lumber in 1978.

- In 1983 a U.S. Department of Agriculture employee experienced internal bleeding followed by complete disability after building picnic tables with treated wood. He sued CCA manufacturers and won more than $700,000 in settlement, discovering in the process that manufacturers had reports of illness from workers sawing treated wood as early as 1968.

- A Washington State schoolteacher was partially paralyzed for three months from arsenic poisoning after building a swimming dock made of wood treated with CCA and settled with manufacturers in 1992.

- A contractor in Bloomington, Ind., suffers from decreased mobility and endured multiple emergency room visits and hospitalizations after getting splinters in his shin while building a deck with treated wood in 1996.

It is becoming increasingly clear that CCA-treated wood presents greater health risks than previously recognized. Moreover, these risks warrant an emergency ban of CCA-treated wood use in playground equipment and an immediate assessment of the safety of treated wood for general use.

4. Many exposure pathways besides manufactured playground equipment exist and need to be addressed.

The 1990 CPSC study examined the risks posed to children playing on manufactured playground equipment. Other studies (e.g CADHS 1987, Roberts and Ochoa 2001) examining the risks associated with arsenic ingestion from CCA-treated wood performed similar focused analyses. However, playground equipment represents only a small fraction of the places where children may come into contact with treated wood.

Pressure-treated wood is ubiquitous. Accounting for nearly a fifth of all softwood boards and timbers sold, treated wood is used not only for children's play structures, but also for decks, railings, picnic tables, fences, docks – basically anywhere wood is used outside. As previously described, almost all of this wood is treated with CCA and therefore is a potential source of arsenic exposure. It is easy to imagine a scenario where children would be coming into contact with treated wood many times during the day. Since kids have a tendency to put their hands in their mouths frequently (an average of 6 and up to 45 times per hour, according to a recent study), it is likely that kids would be ingesting arsenic from each of these sources (Zartarian 1997).

Another exposure pathway that has not been considered by the CPSC and other analyses is soil ingestion. CCA is known to leach from treated wood into the soil below. One study conducted in Connecticut, for example, found levels of arsenic up to 350 parts per million (ppm) and averaging 76 ppm under CCA-treated decks in place for 4 to 15 years. Soils a few meters away averaged only 3.7 ppm (Stilwell and Gorny 1997). Another study of treated wood structures in Florida found the soils underneath to contain up to 217 ppm of arsenic, with an average of 28.5 ppm, while control soils averaged 1.5 ppm (Townsend et al. 2001). The Canadian government found levels of arsenic up to 80 ppm and averaging 50 ppm under CCA treated playground equipment (HWC 1992). These findings have been confirmed by recent tests of soils under municipal play structures in Florida which have shown elevated arsenic levels.

Current analyses that overlook these alternate exposure pathways to arsenic from CCA-treated wood are critically underestimating the risks involved. It is clear that a comprehensive analysis needs to be conducted.

5. Comparable, less toxic alternatives to CCA-treated wood exist.

Safer alternatives to CCA have been used overseas for years and have been gaining acceptance in the U.S. This is a significant change since the EPA last reviewed CCA's registration in 1986, and since the CPSC assessed the safety of CCA treated manufactured play structures in 1990. Wood treated with one alternative chemical, ACQ, is only slightly more expensive than CCA-treated wood, and this price gap is expected to narrow in the future (EBN 2001). Few consumers, however, know of the dangers associated with CCA or the existence of less toxic alternatives.

The most widespread non-arsenic based wood preservative is ammonium copper quat (or ACQ) which is a mixture of copper and didecyl dimethyl ammonium chloride, commonly called quat. Approximately 60 million board feet of ACQ wood was sold in 1998, but a recent agreement by two major wood treatment companies is predicted to significantly expand the availability of ACQ-treated wood (Solo-Gabriele et al. 2000; EBN 2001). ACQ-treated wood is a light tan to olive color, has no detectable odor or vapor, can be painted or stained, and can be used anywhere CCA is used besides marine applications. It has been approved by the American Wood Preservers Association, and was also accepted by the International Conference of Building Officials in 1994 for inclusion in the Uniform Building Code.

Toxicological and ecotoxicological testing has shown that ACQ-treated wood has low mammalian toxicity, and unlike CCA, the chemical contains no EPA-listed compounds and no known or suspected carcinogens (Solo-Gabriele et al. 2000). Although copper (which is also in CCA) is known to be toxic to some aquatic life, quat is used in shampoos and many other human contact applications. Additional alternatives to CCA also

exist, including one other preservative that has been accepted by the International Conference of Building Officials. This chemical, copper boron azole or CBA, has been used extensively in Europe and Japan, but is relatively unknown in the US (Solo-Gabriele et al. 2000). Governor Jeb Bush has recently asked the Florida legislature to stop the use of CCA in the state's own wood treatment plants out of concern over arsenic. A number of wood treatment plants around the US have switched in recent years to using less toxic alternatives.

With comparable, less toxic alternatives already on the market, there is no reason why a lethal and carcinogenic compound should be used for treating wood children and adults are handling daily.

6. The Consumer Product Safety Act and the Hazardous Substances Act require the CPSC to ban CCA for use in playground equipment and promptly review the safety of other uses.

The Consumer Product Safety Act authorizes the CPSC to enact a ban on products which pose "imminent and unreasonable risk of death, serious illness, or severe personal injury" where "no feasible consumer product safety standard would adequately protect the public from unreasonable risk of injury" (15 U.S.C. §2061(a)). The Federal Hazardous Substances Acts "imminent hazard" provision also authorizes a ban on

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Stevenson, Todd A.

From: jonathan held [jsheld@hotmail.com]

Sent: Monday, August 20, 2001 8:55 PM

To: cpsc-os@cpsc.gov

Subject: Petition HP 01-3, Petition for Ban on Use of CCA

To whom it may concern:

I searched your web site and found some information on the use of CCA in playground sets. My email is in support of the ban on CCA in playground sets, and I have included some comments that I hope you will consider when a vote on this matter is conducted. Let me summarize as follows:

I purchased a Backyard products Aspen Play Center playset this weekend as a gift for my 2 ½ year old. After literally 10 hours of putting the playset together, that night, for some odd reason, I opted to do some research on the product on the Internet to find out if there were any safety-related concerns that I should be aware of. What I found absolutely shocked and disgusted me.

I found through several web sites (including www.healthybuilding.net and information from the Environmental Protection Agency) that a vast majority of lumber is treated with CCA, an abbreviation for Chromated Copper Arsenate. In addition to its use in lumber for houses, CCA can also be found in many playsets.

The issue here is two-fold:

1. *Studies of CCA use in lumber have concluded that it's both safe to use and it shouldn't be used.* In large part, the finding depends on what study you read (one can't help but to also look at who conducted the report and realize that proponents issuing favorable reports are generally funded by the lumber industry while negative reports come from outside "watchdog" agencies). At the very least, therefore, CCA use in lumber used for any purpose is questionable at best. A recent article in Time magazine (dated July 8th, 2001), entitled Toxic Playgrounds, goes into some detail about this problem, and even more recently, Governor Bush of Florida closed several playgrounds because excessive amounts of arsenic were detected in the soil. What really angers me is that retail stores, such as Toys R Us, are selling products that have potential health-associated risks and are not disclosing this to consumers. Moreover, the product itself had no warning that the lumber it used was treated with CCA, and when I called Backyard Products (1-800-463-3213) to ask why there was no disclosure, they simply told me that the law didn't require it. How many kids have to die before it becomes a law to disclose such information?

2. *The second issue is that CCA use in lumber should be disclosed - period.* There is information on the EPA home page (do a search on CCA) that discusses precautions that the EPA mandated for workers using CCA treated wood. It boils down to the fact that if I ever were to sand the playset and repaint it, or round off edges using a sander to prevent injury to my child, I would actually be doing more harm then good (to myself and my child), a danger unbeknownst to most people. This is absolutely intolerable, and I find myself in disbelief that we can allow sales of CCA treated lumber to continue without informing the consumer of the dangers in using it. It is apparent that companies are taking advantage of the lack of any law to sell dangerous products.

I ask that you please vote for the ban of CCA in playsets.

One child that dies from this hazard is one child too many, and nothing - not even litigation - will ever bring that child back. And when voting, please ask yourself if you are willing to let your child play on equipment that may be potentially unsafe.

Sincerely,

Jonathan S. Held

Joseph Prager
9409 SW 81st Way
Gainesville, FL 32608
Mail@bancca.org

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Transmittal

2001 AUG 22 P 5:12

To:	Mrs. Ann Brown, Chairperson	**Fax:**	
From:	Joseph Prager	**Date:**	08/20/01
Re:	Petition HP 01-3	**Pages:**	Several; 5 copies included
CC:	Office of Senator Bill Nelson, Dr. Jennifer Howse, March of Dimes, John Ruddell, Florida DEP		

☐ Urgent x For Review ☐ Please Comment x Please Reply ☐ Please Recycle

Notes: Please find attached 5 copies of my letter responding to Petition HP 01-3: "Petition for Ban on Use of CCA Treated Wood in Playground Equipment", for your review and comment. I have also included 5 sets of a study article. *"The role of arsenic as a reproductive toxin with particular attention to neural tube defects"*. Please review this vital information at your earliest opportunity.

Thank you for your time and your consideration.

CCA petition comment 18

August 20, 2001

Mrs. Ann Brown, Chairperson
U.S. Consumer Products Safety Commission,
Washington, DC 20207-0001

RE: Petition HP 01-3: Petition for Ban on Use of CCA Treated Wood in Playground Equipment

Dear Chairperson Brown:

I strongly urge you to grant the petition for rulemaking filed by the Healthy Building Network and the Environmental Working Group, which seeks a ban on CCA-treated lumber products used in playground equipment and requests a safety review of CCA-treated lumber products in general.

This petition is of the utmost importance for several reasons, many of which are detailed in the responses filed by other environmental organizations and interested parties. As owner of the upcoming Web site, www.bancca.org, I am writing to address additional points not covered by these responses, and to offer further important and relevant information on CCA-treated lumber products that bears further investigation by your agency.

I request that you forward this additional information to the CPSC's Office of Hazard Identification and Reduction for use in their review of the safety of CCA-treated lumber for general use by consumers.

In addition to the concerns raised by other organizations about CCA-treated lumber, I would like to bring the following points to your attention:

1. The Teratogenic Effects of Arsenic and Chromium:

There are serious concerns with regard to both arsenic and chromium, two of the primary chemical components of CCA (Chromated Copper Arsenate), and their potential to cause birth defects in both laboratory animals and humans. Numerous studies have been published since the early 1940s on the teratogenic effects of these toxic compounds (References – section 1). Several of these studies show that both arsenic and chromium (CR^6) can cause a wide variety of birth defects in laboratory animals, such as chickens, rats, hamsters, mice and rabbits. In fact, both compounds are listed as known teratogens in the reference manual, **"Catalog of Teratogenic Agents, 9th edition"** by Dr. Thomas Shephard.

Furthermore, one study article on arsenic in particular, *"The Role of Arsenic as a reproductive toxin with particular attention to neural tube defects"* (Shalat, Walker and Finnel, 1996), serves as a comprehensive review of many of the available studies on the topic of arsenic's potential for reproductive toxicity. I am enclosing a copy of this important study, originally published in the *Journal of Toxicological and Environmental Health* for your reference and review. It reaches the conclusion that **"arsenic should be considered a probable human reproductive toxin".**

Arsenic often gets the most attention in any discussion of the hazards of CCA in pressure-treated wood. Yet, the hazards of chromium, in particular hexavalent chromium (CR^6 - also known as chromium trioxide), have mostly gone unmentioned, even though it is also present in and has been proven to leach from CCA-treated wood (Solo-Gabrielle, Townsend 2001).

It is well established that hexavalent chromium is not only a carcinogen, but is also a teratogen. One study *"Occupational exposure to chromium, copper and arsenic during work with impregnated wood in joinery shops"*, (Annals of Occupational Hygiene, 1992), stated the following: "Dust from commercially available [CCA] impregnated wood has been found to contain hexavalent chromium, which is regarded as a carcinogen." Therefore, this same dust is also a probable teratogen.

It recently became known that in standard leaching tests, the toxicity of arsenic and chromium compounds in CCA-treated lumber increases as the particle size decreases (Solo-Gabrielle, Townsend 2001), causing controversy as to whether CCA sawdust should be handled and regulated as a hazardous waste. Moreover, use of deck brightner products by consumers to enhance the appearance of CCA lumber projects, causes a chemical reaction that releases even more hexavalent chromium at the surface, increasing the amount of potential exposure to hexavalent chromium. (Solo-Gabrielle, Townsend 2001).

So, while the focus of the media has been upon the hazards of exposing children to arsenic through playground equipment and CCA-contaminated soil, the research data I have uncovered indicates a serious problem with both arsenic and chromium (CR^6) and their potential effects on animal and human reproductive health. ***Therefore, the greatest risk may not be in exposing children to these carcinogenic compounds, but may instead be in exposing pre-pregnant, pregnant or nursing women to CCA-treated lumber, mulch or sawdust!***

Furthermore, since there are now more women in construction-related jobs traditionally held by men, and since men often have their wives or girlfriends assist them with their do-it-yourself home building projects, the exposure of women to CCA-treated lumber products has increased. Now more than ever before, women end up handling CCA-treated products, and breathing the sawdust from CCA lumber. The question remains: Are women at risk of reproductive harm from exposure to arsenic and chromium?

Evidence from a number of laboratory studies detail the reproductive hazards to laboratory animals of exposure to arsenic and hexavalent chromium. The studies indicate that exposure to arsenic or hexavalent chromium has the potential to cause severe congenital malformations, such as neural tube defects (NTDs), cleft palate, cleft lip, chromosomal damage, and other anomalies in laboratory animals, and even spontaneous abortions in humans (References – section 1). The importance of these studies cannot be overemphasized. In addition, one recent report noted that humans have been found to be much more sensitive than most laboratory animals to the toxicity of arsenic, by a factor of nearly 3000 times in some instances (Solo-Gabrielle, Townsend 2001).

2. CCA – A Potential Endocrine Disruptor:

New information is coming forward about arsenic's potential as an endocrine disruptor, as mentioned in the EWG/HBN petition. One new study, (Kaltreider, et al. 2001) published in the journal *Environmental Health Perspectives*, details how arsenic affects the glucocortoid receptors within the nucleus of the cell itself. It states that *"very low levels of arsenic - equivalent to about 10 parts per billion"* can cause effects inside the cell that *"alter hormonal function in the glucocortoid system"*.

The Florida Center for Solid and Hazardous Waste Management, whose groundbreaking work on how arsenic and chromium leach from pressure-treated wood has helped to bring the hazards of CCA-treated lumber to the foreground (Solo-Gabrielle, Townsend 2001), detailed in their Technical Advisory Group meeting on July 9th that they are also planning further research testing this year on CCA as a endocrine disruptor using hormonally active chemical assays.

3. Voluntary Warnings are Not Sufficient Protection:

When a consumer purchases CCA-treated lumber, he or she is not warned about the potential dangers of these carcinogenic and teratogenic compounds contained in the product, so that an informed decision can be made. Wood industry literature given to consumers touts this product as having *"no risk to human health"* and calls CCA lumber a *"very safe product"* (AWPI brochure 2001). However, the research data, the Material Safety Data Sheet (MSDS) on the product, and numerous Health Department publications point to other conclusions (References - section 3).

Even if a consumer wanted to be proactive about avoiding exposures to toxic chemicals and pesticides - perhaps due to health reasons, or an upcoming pregnancy - there is insufficient information available to the typical consumer to inform them that CCA-treated wood is a product containing potentially harmful chemicals.

While doing research for my Web site, I have personally inspected several of the major home and lumber supply company stores in several states, and have found only one store here in the Gainesville, Florida that is making an attempt to inform its customers of the potential hazards of CCA-treated lumber by posting the MSDS sheets and other wood treatment industry flyers.

Clearly, the voluntary efforts of the wood industry and the lumber retailers are not working and are not a sufficient safeguard for the general public who are being exposed to these toxic compounds. Moreover, the consumer ends up an unknowing and unwitting guinea pig.

4. Transporting CCA is a Serious Risk:

Another seldom mentioned risk is the hazards associated with transporting the CCA chemical formula to wood treatment facilities around the United States. Whether this transportation occurs by cargo ship, railcar or truck, the risk is the same- one careless accident could cause a devastating environmental impact on the affected area or community, threatening its citizen's lives, health, and their water supply.

Since the formula for CCA consists of approximately 22% arsenic (Solo-Gabrielle, Townsend 2001), it is difficult to imagine the total impact that a spill from a tractor-trailor or railroad car filled with CCA could cause. In fact, in a shipping accident in January 1992 off the Eastern seaboard, the *Santa Clara* lost four large containers filled with arsenic trioxide. Similarly, a railroad tank car failure in a rail yard in Chattanooga, Tennessee in 1994 led to the release of a large quantity of arsenic acid, which at first went undisclosed (References – Section 4).

The recent rail accident in downtown Baltimore, along with the tractor-trailer chemical spill this month in downtown Chicago, reminds us all that these kinds of accidents can affect any community at any time. These risks must also be considered.

5. CCA Disposal- a Hidden Cost for Landfills and Local Governments:

Finally, there is a great deal of new data available on the hidden cost of the disposal of CCA-treated lumber. Many municipalities have begun to place bans on its use in public works projects and landfills are now banning disposal of CCA products at their facilities. Unfortunately, owners of private and municipal landfills will end up carrying the added cost burden of proper disposal of CCA-treated products – not the manufacturer. Since CCA-treated lumber cannot be burned without releasing deadly arsine gas, the only "safe" method of disposal at present is to throw discarded CCA lumber in a lined landfill.

Current research indicates that as much as 50% of the disposed wood products in our waste stream contain CCA (Solo-Gabrielle, Townsend, et. al. 2001). While technology now exists in a prototype stage to accurately sort and identify CCA lumber from regular lumber at the landfill's processing centers - using computer-controlled laser spectographic equipment - funding cuts prevent this kind of new technology from being implemented on a large scale.

This means that hundreds of tons of worn-out CCA-treated lumber will be clogging landfills in the next few decades, with little or no opportunity for reclamation or recycling. In Florida alone, the amount of arsenic in disposed CCA-treated wood in our waste stream will amount to almost 27,000 tons (Solo-Gabrielle, Townsend 2001)! CCA lumber waste will rapidly become a disposal nightmare for counties, municipalities and businesses throughout the United States.

Summary:

In conclusion, CCA-treated lumber is no longer the "miracle product" of the 1970s, as new research raises many concerns about the safety of this product. These concerns include:

1. CCA-treated wood product chemicals, including both arsenic and hexavalent chromium, present hazards to the public as carcinogens, teratogens and possible endocrine disruptors.
2. The general public is being exposed to this product without being properly informed of the possible hazards of this product. Voluntary labeling is not working.
3. There are risks associated with the transportation via railway, roadway or waterway of the chemical compounds used to manufacture CCA and CCA itself.
4. The costs and problems associated with the safe disposal of CCA wood are staggering.

Considering that there are now safer alternative wood treatment compounds, such as ACQ, available immediately for effective wood treatment, it is time for the U.S. Consumer Product Safety Commission to place a outright ban on the sale and manufacture of all CCA wood products. This is the only way to truly ensure the public safety.

Thank you for taking the time to consider this vital information.

Sincerely,

Joseph S. Prager
Gainesville, FL
mail@www.bancca.org

CC: Ms. Bridget Walsh, Office of the Honorable Senator Bill Nelson
Dr. Jennifer Howse, President, The March of Dimes
John Ruddell, Florida Department of Environmental Protection

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Role of arsenic as a reproductive toxin with particular attention to neural tube defects.

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Abstract:

Arsenic has been recognized as a human toxicant for over 2000 years. More recently it has been readily accepted as a human carcinogen. Animal research has demonstrated **arsenic**'s ability to have profound detrimental effects on the developing embryo in avian and mammalian species. This article comprehensively reviews the human and animal literature on the subject of the reproductive toxicity of **arsenic**. A variety of endpoints are considered, including spontaneous abortion, cardiovascular defects, and **arsenic**'s role in the causation of neural tube defects (NTDs). A summary of the literature that has examined the various postulated mechanisms by which **arsenic** may produce NTDs is also considered. In addition, a discussion of literature relative to the presence of **arsenic** in the general environment and in the workplace is presented. This article reaches the conclusion that while further research is clearly needed, particularly on the potential toxicity of organic arsenical compounds, the current literature suggests it may be prudent and appropriate to treat inorganic **arsenic** as a probable human reproductive toxin.

Medical Subject Headings (MeSH):

Animal
Arsenic/*TOXICITY
Environmental Exposure
Human
Neural Tube Defects/*CHEMICALLY INDUCED
Neural Tube Defects/*EPIDEMIOLOGY
Neural Tube Defects/*ETIOLOGY
Neural Tube Defects/*GENETICS
Poisons/*TOXICITY
Reproduction/*DRUG EFFECTS
Support, Non-U.S. Gov't
Support, U.S. Gov't, P.H.S.
Teratogens/TOXICITY

Substance (CAS Registry Number):

Poisons (NO CAS RN)
Teratogens (NO CAS RN)
***Arsenic (7440-38-2)**

Language: English

International Standard Serial Number: 0098-4108

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ROLE OF ARSENIC AS A REPRODUCTIVE TOXIN WITH PARTICULAR ATTENTION TO NEURAL TUBE DEFECTS

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Arsenic has been recognized as a human toxicant for over 2000 years. More recently it has been readily accepted as a human carcinogen. Animal research has demonstrated arsenic's ability to have profound detrimental effects on the developing embryo in avian and mammalian species. This article comprehensively reviews the human and animal literature on the subject of the reproductive toxicity of arsenic. A variety of endpoints are considered, including spontaneous abortion, cardiovascular defects, and arsenic's role in the causation of neural tube defects (NTDs). A summary of the literature that has examined the various postulated mechanisms by which arsenic may produce NTDs is also considered. In addition, a discussion of literature relative to the presence of arsenic in the general environment and in the workplace is presented. This article reaches the conclusion that while further research is clearly needed, particularly on the potential toxicity of organic arsenical compounds, the current literature suggests it may be prudent and appropriate to treat inorganic arsenic as a probable human reproductive toxin.

Arsenic has been recognized as a human toxicant for over 2000 years. Tales of the Middle Ages denoted the element as an acute lethal poison to both humans and pests, while medical studies in the sixteenth century linked chronic exposure to ulcerative skin lesions (Buchanan, 1962). Chronic environmental exposure to the metalloid

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has been found to cause human cutaneous and visceral cancers, peripheral neuropathy, microangiopathy, bone marrow and immune suppression, and cardiovascular disease (Winship, 1984; IARC, 1980; Burns et al., 1994; Smith et al., 1992). Even though arsenic occurs naturally in rock formations and thus in groundwater, these latter conditions have been observed concurrent with the expansion of industrial utilization of arsenic and resulting environmental contamination (Buchanan, 1962; Stohrer, 1991; Winship, 1984). Currently, much research is being directed toward clarifying the potential for and molecular mechanisms involved in the toxicity, particularly in reproductive outcomes of each conformational form of arsenic.

Prior to the development of antibiotics, medicinal applications, such a cacodylic acids, were a significant source of human exposure to arsenic. In the early 1930s, in association with its use against the spirochete of syphilis, arsenic was shown to be retained by the fetal portion of the placenta of treated pregnant women (Eastman, 1931). Arsenic is now known to readily cross the placental barrier and selectively accumulate in the fetal neuroepithelium during early embryogenesis (Hanlon & Ferm, 1977; Lindgren et al., 1984). Various fetal malformations have been observed in animals following embryonal arsenic exposure. Neural tube defects (NTDs) appear as a predominant and consistent outcome in multiple mammalian species (Mottet & Ferm, 1983; Willhite & Ferm, 1984). In humans, prenatal exposure to acute high doses of arsenic has resulted in miscarriage and early neonatal death (Bolliger et al., 1992; Lugo et al., 1969). Prolonged low-dose human arsenic exposure has been associated with multiple adverse reproductive outcomes including spontaneous abortion, stillbirth, developmental impairment, and congenital malformation (Aaschengrau et al., 1989; Borzsonyi et al., 1992; Beckman, 1978; Zierler et al., 1988). The association between human prenatal arsenic exposure and congenital malformations including NTDs has not yet been fully resolved. However, given the abundance of data supporting arsenic's teratogenic potential in multiple species, it seems unlikely that humans are uniquely insensitive to such adverse effects.

DESCRIPTIVE EPIDEMIOLOGY AND PATHOLOGENESIS OF HUMAN NEURAL TUBE DEFECTS

Congenital malformations are found in 4–8% of all live births (Keeling & Boyd, 1993). The prevalence of NTDs, which result in major malformation of the brain and/or spinal cord, varies widely in different geographical areas from fewer than 4 per 10,000 live births (Central-East France) to over 20 per 10,000 live births (Mexico, Northern Ireland) (WHO, 1991). A high prevalence of NTDs has been reported in regions of Scotland, Wales, India, Pakistan, the Middle

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East, and northern China (Laurence, 1993). The incidence of NTDs in stillborn and aborted fetuses is unknown, but it is likely at least as frequent as in livebirths, especially where improved antenatal diagnosis of the defect is decreasing the incidence of full-term affected fetuses (Bower et al., 1993). For unknown reasons, a higher number of cases of NTDs is usually reported in female than in male infants (Campbell et al., 1986). The most readily recognized of the NTDs are dysraphic spina bifida and anencephaly. Approximately twice as many infants are born with spina bifida than with anencephaly, a ratio that may be partly determined by the greater ease in antenatal diagnosis of anencephaly (Keeling & Boyd, 1993). Anencephaly is a result of incomplete closure of the cranial portion of the neural tube, which leads to an open cranial vault (acrania), aplasia of cerebral hemispheres, and defective development of other brain structures (Laurence, 1993). A more severe form of this NTD, occurring in approximately 50% of anencephalic cases, is craniorachischisis, which is an open fissure involving both brain and some or all of the spinal cord (Laurence, 1993). Anencephaly is usually an isolated defect, but is sometimes reported with other malformations, such as cleft palate and cardiovascular or renal anomalies (Martin et al., 1983). Spina bifida occurs with incomplete fusion of the neural tube below the level of T12. The extent of the defect can vary from a short segment of unfused neural folds covered by a locally exposed meningeal sac (myelocoele), to a complete longitudinal fissure of the spinal cord with absence of meningeal development (myeloschisis) (Laurence, 1993). Infants with spina bifida have varying degrees of neurologic dysfunction.

Neural tube defects originate in early embryogenesis during the process of neurulation. This process occurs over a limited number of embryonal stages, and is divided into primary and secondary phases (Muller & O'Rahilly, 1987). Primary neurulation occurs by folding and fusion of a specialized plate of epithelial cells that give rise to the brain and most of the spinal cord. Four distinct closure sites of the primary neural tube have been recognized in both laboratory rodents and humans (Busam et al., 1993; Golden & Chernoff, 1993, 1995; Kaufman, 1979; Van Allen et al., 1993). Each closure site is believed to be independently and differentially susceptible to interference by teratogens, potentially explaining the site specificity of selected neural tube toxicants.

THE VARIED ETIOLOGY OF HUMAN NEURAL TUBE DEFECTS

Multiple diverse etiologic factors have been implicated in the development of human NTDs, including maternal hyperthermia, impaired folate metabolism, and gestational exposure to retinoic acid and its derivatives or certain anticonvulsant drugs (Fisher & Smith,

1981; Milunsky et al., 1992; MRC Vitamin Research Study Group, 1991; Lemire, 1978; Lindhout et al., 1992; Scott et al., 1994). Neural tube defects have also been attributed to chromosomal defects as well as single gene determined syndromes such as Meckel–Gruber syndrome (Hall et al., 1988; Holmes et al., 1976). The mechanism(s) by which exogenous factors interfere with neural tube closure is generally unknown. However, neural tube closure appears to be dependent upon specific, integrated cellular responses with which teratogens may interfere.

THE MECHANISTIC ROLE OF ARSENIC IN THE PATHOGENESIS OF NEURAL TUBE DEFECTS

Certain xenobiotics that interfere specifically with cellular replication can induce NTDs in rodent embryos (Elwood & Elwood, 1980; Lee et al., 1972), and reduced cell proliferation at specific sites of NTDs has been demonstrated in mouse strains that have a high prevalence of spontaneous NTDs (looptail, curlytail) (Copp et al., 1988; Brook et al., 1991; Wilson & Center, 1974). Arsenic may induce developmental malformations similarly, as proliferation of human fetal and other mammalian cells is inhibited by in vitro and in vivo arsenic exposure (Dong & Luo, 1993; Jha et al., 1992; Petres et al., 1977). Inorganic arsenic impairs assembly and disassembly of microtubules, presumably by binding to protein sulphydryl groups, and thus may interfere with mitotic spindle formation and embryonal cell division (Leonard & Lauwerys, 1980; Li & Chou, 1992; Mottet & Ferm, 1983). Arsenicals further cause chromosomal aberrations (Jha et al., 1992; Leonard & Lauwerys, 1980), which disrupt cell cycling, thereby reducing the organism's capacity for cellular proliferation.

Specific neuroepithelial cell shape changes are also essential to the process of neurulation (Moriss-Kay et al., 1993). Lateral neural plate cells become elongated, then wedge shaped during folding. Extension of vertically oriented microtubules and contraction of apical microfilaments are believed to effect these individual cell shape changes, while contraction of neuroepithelial cell basal microfilaments may act to maintain the biconvexity of the peripheral neural folds (Gunn & Juriloff, 1992). Controlled intercellular adhesion and cytokinesis, mediated by polymerization and depolymerization of cytoskeletal elements, also appear to be critical for neural tube formation (Edelman, 1992; Schoenwolf & Smith, 1990). These cytoskeletal elements are functionally affected by alterations in their protein sulfhydryl groups, protein phosphorylation reactions, and intracellular ion concentrations, all of which are affected by arsenic oxides (Dallaire & Beliveau, 1992; Li & Chou, 1992; Taubeneck et al., 1994). Exposure to even relatively low concentrations of inorganic arsenic has recently been shown to have a

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Increased and unregulated cell death has been proposed as a mechanism of arsenic-induced teratogenesis (Mottet & Ferm, 1983). The cytotoxicity of arsenic trioxide (arsenite) is at least partially due to its ability to form cyclic adducts with sulfhydryl groups of certain enzymes, resulting in abrupt inhibition of glycolysis and beta-oxidation (Muckter et al., 1993; Knowles & Benson, 1983; Rein et al., 1979). The substitution of pentavalent arsenic (arsenate) for phosphorus in mitochondria uncouples oxidative phosphorylation, presumably effecting the acute high-dose cytotoxicity of this valency form (Webb, 1966). At low doses, the metabolic effects of either valency form may be selectively detrimental to the developing embryo and fetus. Fetal blood glucose is 30–40% less than maternal values (Fowden, 1994). This factor, coupled with the obligate high glucose requirement of the fetal neuroepithelium, may predispose this tissue to the metabolic toxicity of arsenic. The cytotoxicity of arsenic is also a consequence of the oxyanions affinity for sulfhydryl groups of histones and nucleic acids, a reaction that may be responsible for inducing the chromosomal damage well documented in both in vitro and in vivo arsenic-exposed cells (Jha et al., 1992; Dong & Luo, 1993; Leonard & Lauwerys, 1980). The chromosomal aberrations observed in fetal cells following maternal arsenic exposure (Nagymajtenyi et al., 1985) particularly suggest this latter mechanism may be involved in the teratogenicity of the element. Similar media concentrations of arsenic also inhibit in vitro cellular DNA reparative enzymes (Li & Rossman, 1989), reduce cytosolic glutathione levels, and induce membrane lipid peroxidation (Huang et al., 1993; Tabacova et al., 1994a), suggesting multiple mechanisms may be involved in arsenic induced cytotoxicity, fetotoxicity and teratogenicity. In a study of 49 maternal–infant pairs (Tabacova et al., 1994b), a high degree of correlation ($r^2 = .71$) was observed between environmental arsenic and placental arsenic levels. This study went on to also observe that the combined effect of smoking and living near the smelter area was associated with lower glutathione antioxidant protection. This in turn resulted in observed higher levels of lipid peroxides in maternal blood, cord blood, and placenta, suggesting that fetuses of these women, with both exposures, may be at increased risk of oxidative damage.

Altered placental and/or embryonal vasculature and nutrient supply have long been suggested mechanisms leading to NTDs. In humans, prolonged low-level arsenic exposure is a known cause of microvascular injury (Tseng, 1977) and in particular to the incipient vasculature of the placenta; thus the embryo may be especially vulnerable to this form of toxicity. The lack of endothelial intercellular tight junctions to create an effective blood–brain barrier in the fetus indicates greater

susceptibility to circulating arsenicals of prenatal, compared to postnatal, neuronal tissues.

Additionally, arsenic has been shown in diverse in vitro studies to alter transcellular, transcapillary and transplacental transport of various nutrients (Dallaire & Beliveau, 1992; Deneke, 1992; Taubenek et al., 1994; Widnell et al., 1990), and in vivo to decrease fetal zinc levels, possibly through induction of maternal metallothionein synthesis (Taubenek et al., 1994). This latter effect may be particularly significant in that low fetal zinc levels have been shown to be teratogenic in humans (Cherry et al., 1981; Jameson, 1976) and to result specifically in NTDs in rodents (Warkany & Petering, 1972).

Further, deficiencies of select nutrients have been proposed to enhance the teratogenic potential of arsenic (Ferm & Hanlon, 1986; McKinney, 1992; Vahter & Marafante, 1987). Arsenic is detoxified by hepatic methylation to organic arsenicals (Buchet & Lauwerys, 1987; Hood et al., 1987, 1988; McKinney, 1992; Thompson, 1993), and the cofactor, *S*-adenylmethionine (SAM), is considered the fundamental methyl donor in this pathway (Buchet & Lauwerys, 1987; Vahter & Marafante, 1987; Thompson, 1993). Methionine and protein deficiencies are thought to decrease availability of this cofactor, and have been shown to result in increased tissue retention of inorganic arsenic in vivo (Vahter & Marafante, 1987). Such nutrient deficiencies concomitant with prenatal exposure to arsenic or similarly metabolized teratogens provide an explanation for the comparatively higher incidence of NTDs typically reported among families of lower socioeconomic classes. Vitamins B_{12} and folate are also required for the synthesis of SAM. There is currently great scientific interest in these latter two vitamins and their role in altering the risk of NTDs. The decreased incidence of NTDs reported in the offspring of women provided early gestational folate or folate/vitamin B_{12} supplementation (MRC Vitamin Research Study Group, 1991; Brouwer et al., 1992) may be a result of indirectly enhanced tissue levels of SAM, precluding inordinate retention of arsenic or similarly metabolized teratogens. Regardless, clearly folate deficiency is an important risk factor for NTDs; if and how arsenic may be an independent or synergistic factor requires further investigation.

GENETIC MECHANISMS IN THE PATHOGENESIS OF NEURAL TUBE DEFECTS AND ARSENIC TOXICITY

Altered gene expression has been observed with, and may have a causative role in, the induction of NTDs following prenatal exposure to certain teratogens, including arsenic. Transient maternal hyperthermia induces expression of a select group of heat shock proteins (hsps) and specifically results in NTDs in laboratory animals (Mirkes & Cornel,

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1992). Arsenic-exposed rat embryos have recently been shown to express the same pattern of heat shock proteins as hyperthermia-treated embryos (Mirkes & Cornel, 1992). Further, prenatal arsenic exposure synergistically increases the incidence of NTDs following maternal hyperthermia (Ferm & Kilham, 1977; Hanlon & Ferm, 1986). However, the neural tube malformation induced by arsenic exposure alone differs morphologically from that induced by maternal hyperthermia, suggesting that factors other than the classic heat shock response are involved (Mirkes & Cornel, 1992). This synergism has also been noted with a combination of administration of sodium arsenate plus restraint (Rasco & Hood, 1994). Significantly increased rates of exencephaly and decreased fetal weight were seen in the group exposed to both factors. Amplification of select genes in cells exposed to arsenic in vitro and decreased expression of certain developmental genes in embryos exposed to arsenic in vivo and in vitro have been repeatedly demonstrated (Lee et al., 1988; Fang et al., 1993; Craig et al., 1995). Thus, the specific and consistent pattern of arsenic-induced NTDs may be explained on the basis of selective alteration in embryonic gene expression, especially if such critical developmental determinants as homeobox genes and intercellular adhesion molecules are involved. Arsenic has also been recently shown to selectively inhibit methylation of cellular proteins (hsps), potentially interfering with posttranslation regulation of proteins that have a critical role in embryonic development (Wang et al., 1992).

Inherited susceptibility to NTDs is considered an important factor affecting outcome of human prenatal exposure to a wide variety of teratogens. Multiple studies have documented variation in susceptibility to several neural tube teratogens among inbred strains of mice. Finnell et al. (1986, 1988, 1993) have specifically shown a significant difference between inbred mouse strains in terms of their susceptibility to hyperthermia and chemically induced NTDs. Relative susceptibility of the different strains to hyperthermia-induced NTDs was found to be similar to that of chemically (valproate) -induced NTDs. Genetic susceptibility for NTDs among inbred mouse strains to teratogenic effects of lead and cadmium has also been reported (Gale & Layton, 1978; Layton & Layton, 1979). To date only species but not strain differences to the teratogenic effects of inorganic arsenic have been demonstrated (Ferm & Hanlon, 1983; Tabacova & Hunter, 1993). In humans, NTDs appear to be more common among certain ethnic groups suggesting some degree of inherited susceptibility (Hall et al., 1988). Furthermore, once an individual has given birth to one child with an NTD, she has a threefold increased recurrence risk, and siblings of affected infants have a 10-fold increased risk of having offspring with NTDs. Taken in light of the fact that there is a significant increase in the incidence of consanguinity amongst females with NTDs, the evi-

dence is strong that hability genes clustering in such sibships have a major contribution to the overall NTD risk. Nonetheless, common dietary patterns, diseases, and environmental conditions may also be culturally determined factors.

ARSENIC AS A TERATOGEN: ANIMAL STUDIES

Arsenic has been considered a teratogen since the early 1940s, when chick embryos were found to develop a variety of malformations following low-level arsenate exposure (Ancel & Lallemand, 1941). Similar studies have further documented these results. In a recent report, chick embryos exposed to arsenic in vitro had increased incidence of everted viscera, microphthalmia, and embryonic death (Gilani & Alibhai, 1990). Prenatal arsenic exposure in mammals induces a predominant pattern of fetal NTDs, specifically encephaloceles and exencephaly (the animal equivalent to anencephaly). This has been a consistent outcome in over 30 studies involving laboratory rodents, including hamsters (Ferm & Carpenter, 1968; Harrison & Hood, 1981; Hood et al., 1988), mice (Chaineau et al., 1990; Muller et al., 1986), and rats (Umpierre, 1981). Cleft palate and skeletal, ophthalmic, and urogenital malformations have additionally, although somewhat variably, been induced in mice and rats. Fetal growth retardation as well as embryonic death are generally increased following prenatal arsenic exposure in all laboratory species. Abnormal neurological development in neonatal mice prenatally exposed to low doses of inorganic arsenic has recently been reported (Ma et al., 1994).

ARSENIC IN THE ENVIRONMENT

Arsenic is nearly ubiquitous in the environment, being derived from both natural and anthropogenic sources (Muller et al., 1986). In fact the highest levels of arsenic in drinking water are often the result of soil or rock with high natural levels. However, concentrations of arsenic compounds in drinking water supplies and soils can be the result of industrial contamination (Pershagen, 1986; Smith et al., 1992). Atmospheric arsenic from industrial sources is estimated to be nearly 30 times that from natural sources on a global scale (Lantzy & MacKenzie, 1979). Multiple valency states of inorganic arsenic are found in the environment. Pentavalent arsenic (arsenate) generally predominates in soils, while trivalent arsenic (arsenite) predominates in airborne particulates from both smelter stack dust and pesticides, the two major sources of atmospheric arsenic (Pershagen, 1986). Trivalent arsenic is considered more acutely toxic and embryolethal in laboratory animals than is the pentavalent form. Arsenate generally induces fetal malformations with less embryonic mortality and maternal toxicity, and

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for these reasons is more often incorporated in studies of the element's teratogenicity. Organic forms of arsenic are a variable source of human exposure, being derived primarily from meat (secondary to the use of arsenic in the form of arsanilic acid as a feed additive, particularly for poultry) and seafood. Marine organisms, especially bottom-feeding crustaceans, bioconcentrate arsenicals (primarily in the form of arsenobetaine and arsenocholine), so that a recent meal of shellfish can substantially increase a person's measured urinary arsenic level (Pershagen, 1986). These organic compounds appear to be relatively non-toxic compared to inorganic arsenic. However, methylarsenicals have been shown to bind to intracellular thiol groups and cause oxidative tissue injury and should not be considered nontoxic (McKinney, 1992).

Studies have shown significant inter-species variation in the metabolism of inorganic arsenic (Vahter, 1994). In humans exposed to inorganic arsenic 10–30% is directly excreted as the inorganic form, 10–20% as methylarsonic acid, and 60–80% as dimethylarsinic acid (Hopenhayn-Rich et al., 1993). Mice are far more efficient in methylating arsenic than humans (Vahter, 1981). Rats are similarly efficient, but store a significant portion of the dimethylarsinic acid in their erythrocytes (Hunter et al., 1942; Stevens et al., 1977; Odanaka et al., 1980). Among common laboratory animals it appears that the rabbit and the hamster are more similar to humans in their metabolism of arsenic (Vahter & Marafante, 1983; Yamauchi & Yamamura, 1984, 1985; Marafante & Vahter, 1987). The fact that arsenic is more readily methylated in rodents compared to humans suggests human sensitivity to the teratogenic effects of inorganic arsenic may be greater.

The presence of organic arsenicals in urinary samples, when only total arsenic concentration is assessed (without speciation of the different forms of the metalloid), complicates interpretation of arsenic exposure level (Pershagen, 1986; Smith et al., 1992). Human exposure to the more toxic inorganic forms of arsenic occurs primarily through polluted soil and municipal water supplies (Pershagen, 1986; Smith et al., 1992; Winship, 1984). Inorganic arsenic is a major by-product of nonferrous smelting, and of electrical power plants fueled by arsenic-containing coal (Winship, 1984; Pershagen, 1986). It is also used throughout the world in a wide range of agricultural products including herbicides, insecticides, fungicides, rodenticides, desiccants, and defoliants. The element is a standard ingredient in wood preservatives, glassware, and some medicaments. Although it is increasingly being banned as an ingredient in the pharmaceutical industry, its use is expanding in other enterprises, such as in the manufacture of electronic equipment including computer circuits and lasers (Burns et al., 1994). In addition, human exposure occurs from products indirectly contaminated with arsenic. Pesticide use on grapes can substantially increase

arsenic exposure level of wine drinkers, and its similar use on tobacco can more than double the daily exposure level of cigarette smokers (Pershagen, 1986).

The United States is the single greatest consumer of arsenic processed for industrial use (Winship, 1984). Relatively high arsenic levels continue to be reported in U.S. municipal water supplies (Stohrer, 1991), with an estimated 350,000 U.S. citizens exposed to levels that exceed the U.S. drinking water standard (Smith et al., 1992). Various geographical regions worldwide have persistently and sometimes markedly elevated environmental arsenic concentrations as a result of industrial contamination (Stohrer, 1991; Tseng, 1977). The highest random blood levels recorded have been in persons whose occupation exposed them to airborne arsenic particulates or whose local water supply was polluted with high concentrations of the metalloid. Random human blood levels in the range of concentrations that were embryotoxic and teratogenic to mice have been reported (IARC, 1980).

HUMAN EPIDEMIOLOGIC RESEARCH AND ADVERSE REPRODUCTIVE OUTCOMES

A number of epidemiologic studies (Weisenburger et al., 1992; Munger et al., 1992; Sever et al., 1988; White et al., 1988; Brender & Suarez, 1990; Balarajan & McDowall, 1983; Field & Kerr, 1979) have found associations between increased risk for a number of major congenital malformations and environmental exposure to pesticides. [Pesticide is a broad term used to encompass a vast number of chemical compounds that are used for the control of insect, fungi, weeds, rodents, nematodes, and other pests (Hayes & Lawes, 1991).] Arsenic has been widely used as both a pesticide on a variety of crops and a defoliant in the harvesting of cotton.

Several human epidemiologic papers and case reports have observed increased rates of NTDs in association with exposures to pesticides (Sever, et al., 1988, White et al., 1988; Brender & Suarez, 1990; Balarajan & McDowall, 1983; Field & Kerr, 1979). In the study of communities near Hanford, Washington (Sever et al., 1988), elevated rates of neural tube defects were observed (17.2 per 10,000 births over a 12-yr period in a cohort of 23,000 births). Because of the widespread use of herbicides in this area the authors concluded that further study of the relationship between these chemicals and NTDs was warranted. A study in New Brunswick, Canada, was carried out specifically to look at birth defects and agricultural exposures (White et al., 1988). The authors reported a statistically significant doubling of the number of cases of congenital malformations including anencephaly, spina bifida, cleft palate, cleft lip, and renal agenesis. A

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study of birth defects and paternal occupation in agriculture was conducted in England and Wales (Balarajan & McDowall, 1983). The results indicated a modest increased risk of anencephaly, spina bifida, and cleft lip and/or palate among offspring of gardeners and groundsmen, but not other agricultural occupations. In a study in Texas, Brender and Suarez (1990) reported significantly increased risk of anencephaly in offspring of solvent-exposed workers. Among the other findings of this study was a 28% increase in the risk of neural tube defects in offspring of pesticide-exposed workers, and an increase of 73% in those of farm and ranch workers, although neither of these findings were statistically significant. However, in a case-control study conducted to evalute a cluster of NTDs in Brownsville, Texas, performed by the Texas Department of Health (1992), a statistically significant increase of 330% for NTDs was reported to be associated with aerial spraying of pesticides on crops.

While some information has been obtained in some studies on the use of specific pesticides, in general most epidemiologic studies have little specific qualitative let alone quantitative data on the specific pesticide exposure. Given the widespread historical use of arsenical compounds in agriculture and its persistence in the environment, the possibility that the observed increased risk of NTDs in agricultural populations may be attributable to arsenic should be carefully considered.

Maternal exposure to arsenic can occur from workplace exposures, smoking, diet, and through exposure to contamination of drinking water, housedust, and ambient air (Tabacova, 1986). In exposed mothers, arsenic is present in maternal blood, readily crosses the fetomaternal interface, and accumulates in certain fetal tissues including the placenta at concentrations much greater than that in maternal blood. Fetal blood arsenic levels are increased with gestational time (Eastman, 1931; Lugo et al., 1969).

The first study published by Nordström and co-workers (1978a) retrospectively examined variations in birth weight of the children born to female workers and women living near the Rönnskär smelter in northern Sweden. Results of this study indicate that women employed at the Rönnskär facility, and those women who lived within 10 km of the plant, gave birth to children with lower birth weights than those observed in a control population and among women living further away from the plant, presumably due to arsenic, lead, and sulfur dioxide emissions.

In a study published the same year, Nordström and colleagues (1978b) retrospectively examined the frequency of spontaneous abortion occurring in the population living around the Rönnskär smelter. In this case, exposure was determined by proximity of the women's homes to the plant. Results indicated that women living closest to the plant experienced rates of spontaneous abortion that were significantly

greater than those living further away from the facility. Additionally, women living in the area closest to the smelter had a higher proportion of adverse pregnancy outcomes.

In 1979, Nordström and his co-workers published two more studies on adverse reproductive outcomes associated with the Rönnskär smelter. One of these papers (1979a) retrospectively determined birth weights and rates of spontaneous abortion among 511 female employees of the smelter compared to a control population. Status of exposure to arsenic for the women was determined by plant records on the type of work each woman performed. The administered questionnaire collected information on maternal smoking habits, parity, pregnancies, abortions, and gestational age at parturition. Reported pregnancies and abortions were verified by checking medical records. Results of this investigation indicated that the mean birth weight for children born to female Rönnskär employees was significantly lower than that of controls, and that this decrease was most pronounced in later pregnancies. Women who were directly involved in smelting or cleaning processes experienced lower birth weights for all pregnancies. Additionally, women who smoked experienced significantly lower birth weights than nonsmokers. Rates of spontaneous abortion (miscarriage) were highest when the women were employed at the smelter prior to or during pregnancy. Women working directly in smelting and cleaning processes experienced the highest rates of spontaneous abortion of all women included in the study. This rate was increased when the father was also a plant employee. It is important to note that women who work directly in smelting and cleaning processes would experience higher levels of arsenic exposure than other plant employees. This study indicates that arsenic exposure had adversely affected pregnancies in female plant employees.

The second paper published in the same year (1979b) retrospectively examined rates of congenital malformation among female plant employees and rates in the Skellefteå region, which surrounds the Rönnskär smelter. Only employment at the Rönnskär smelter was considered in order to determine exposure status. Results of the study indicated that offspring of females employed at the smelter exhibited increased rates of congenital malformations, and that the increase was fourfold for children with multiple malformations. The authors concluded that this effect was due to direct teratogenicity of toxin exposures at the plant. This group of investigators published one additional study on the reproductive outcomes of employees of the Rönnskär smelter (Beckman & Nordström, 1982). This investigation centered on fetal mortality among the wives of men employed at the Rönnskär facility. The study observed that rates of stillbirth (fetal mortality) were significantly higher among the exposed workers than among nonexposed

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workers. The authors suggested that this effect was not due to an alteration of sperm, but could be due to exposure of workers' wives to dust contamination on workers' clothes.

Börzsönyi and co-workers have published the preliminary results of an investigation in which they compared the rates of spontaneous abortion and stillbirth among high-level and low-level arsenic-exposed populations in southeast Hungary over a 2-yr period (Börzsönyi et al., 1992). The preliminary results indicated that the rates of spontaneous abortion and stillbirth were significantly increased in the high-level exposure group. Due to the inclusion of smoking status and occupational information in their study, it is more likely that the differences in reproductive outcomes between these two populations are due to their arsenic exposure patterns.

Zierler and colleagues (1988) performed a case-control study that examined parental exposures and adverse reproductive outcomes. This investigation looked at rates of congenital heart disease in association with drinking water contamination among Massachusetts residents over a 3-yr period. Cases were obtained from the New England Regional Infant Cardiac Registry, and death records for Massachusetts. Many possible maternal exposures, including arsenic, were assessed by examination of public water supply records within 1 yr of an identified pregnancy. Exposure to other possible contaminants and maternal socioeconomic status were corrected in the statistical analysis. The study found an association between arsenic exposure at any level and a 200% increase in risk of coarctation of the aorta.

Critical to interpretation of epidemiological information pertaining to human reproduction is consideration of the potential for multiple "endpoints" or reproductive outcomes from a single teratogen. As demonstrated in animal studies, concentration or dosage, duration, and the time in pregnancy of maternal toxicant exposure, as well as synergism between toxicants, are variables that may affect reproductive outcome. Genetic and nutritional susceptibility may be additional variables. Even when such variables are well controlled in animal studies, a single teratogenic compound, including arsenic, typically results in multiple reproductive endpoints. Therefore, while NTDs appear as a consistent outcome of prenatal arsenic exposure in laboratory studies with rodents, a less consistent and selective pattern of reproductive outcomes should be expected with exposure in humans. Authors of some epidemiological studies and reviews on the reproductive toxicity of arsenic have suggested that maternal exposure to the metalloid may particularly explain many unaccountable early miscarriages. The potential for multiple reproductive endpoints complicates epidemiological studies, but needs to be considered to adequately clarify the reproductive risks of arsenic exposure.

SUMMARY

The reproductive toxicity of acute arsenic exposure has been established, while that of prolonged low-level exposure has yet to be adequately defined. Current opinion among researchers, regulatory agencies, and other pertinent organizations on the reproductive risk to humans from environmental arsenic exposure is often contradictory. In a 1991 publication, the nonregulatory Agency for Toxic Substance and Disease Registry (USPHS/ATSDR), basing risk assessment primarily on human metabolic studies and clinical cases, found the element to be potentially fetotoxic and teratogenic only at doses likely to cause maternal toxicity. However, a 1990 publication of the California Department of Health Services (CDHS/ATES) supported a statement made decades earlier by researchers Hanlon and Ferm (1974) that "to overlook the teratogenicity of arsenic compounds on the basis of maternal toxicity would be inappropriate because the compounds appear to have specific targets in the developing organism." The Committee on Medical and Biological Effects of Environmental Pollutants, National Academy of Sciences (1977), noted that humans may be even more sensitive to the adverse reproductive effects of arsenic than are standard laboratory species. This latter conclusion is likely derived from the fact that rodents are more efficient methylators and more completely detoxify inorganic arsenicals than humans (Hughes et al., 1994, McKinney, 1992). Within the scientific community, arsenic is known to be a carcinogen, potential human teratogen, and possible cause of human NTDs. Considering the widespread contamination and persistence in the environment, and continuing industrial use of the element, further research on the metalloid's potential toxicity to human reproduction is essential. While future studies should investigate the specific mechanisms of arsenic-associated teratogenesis and all potential reproductive outcomes of human arsenic exposure, arsenic should be considered a probable human reproductive toxin.

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